THERAPEUTIC METHODS AND COMPOSITIONS

FIELD

[0001] Disclosed herein are therapeutic methods and compositions utilizing placental stromal cells.

BACKGROUND

[0002] Metabolic syndrome, also known as syndrome X or dysmetabolic syndrome, refers to a cluster of metabolic conditions that can lead to heart disease, retinopathy, nephropathy, neuropathy, and a host of other sequelae. Features of metabolic syndrome include insulin resistance, hypertension, an abnormal cholesterol profile, and an increased risk for clotting. People diagnosed with this syndrome are usually overweight or obese. Insulin resistance is a condition in which the body produces insulin but does not respond to it properly. Improved therapies for these conditions are urgently needed in the art.

SUMMARY

[0003] Provided herein are methods of ameliorating and treating elevated blood glucose levels, Impaired Glucose tolerance (IGt), systemic inflammation, and sequelae thereof, in subjects with obesity and metabolic disorders, such as T2DM and metabolic syndrome, comprising administration of adherent stromal cells (ASC). In certain embodiments, the ASC are derived from a placenta. In other embodiments, the ASC are derived from adipose tissue, or BM. In other embodiments, the ASC are derived from a different source tissue.

[0004] In certain embodiments, the ASC described herein have been cultured on a 2-dimensional (2D) substrate, a 3-dimensional (3D) substrate, or a combination thereof. Non-limiting examples of 2D and 3D culture conditions are provided in the Detailed Description and in the Examples.

[0005] Reference herein to "growth" of a population of cells is intended to be synonymous with expansion of a cell population.

[0006] Except where otherwise indicated, all ranges mentioned herein are inclusive.

[0007] Unless otherwise defined, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this invention belongs. Although methods and materials similar or equivalent to those described herein can be used in the practice or testing of the invention, suitable methods and materials are described below. In case of conflict, the patent specification, including definitions, will control. In addition, the materials, methods, and examples are illustrative only and not intended to be limiting.

BRIEF DESCRIPTION OF THE DRAWINGS

[0008] The invention is herein described, by way of example only, with reference to the accompanying drawings. With specific reference now to the drawings in detail, it is stressed that the particulars shown are by way of example and for purposes of illustrative discussion of the embodiments of the invention only, and are presented in the cause of providing what is believed to be the most useful and readily understood description of the principles and conceptual aspects of the invention. In this regard, no attempt is made to show structural details of the invention in more detail than is necessary for a fundamental understanding of the invention, the description taken with the drawings making apparent to those skilled in the art how the several forms of the invention may be embodied in practice.

[0009] In the drawings:

[0010] FIG. **1** is a diagram of a bioreactor that can be used to prepare the cells.

[0011] FIG. **2** depicts the study visit flow chart for the study described in Example 5.

[0012] FIG. **3** is a chart showing characteristics of placental ASC expanded on 2D substrates, followed by 3D carrier expansion and removal from the carriers. CV % indicates the coefficient of variance, obtained by dividing the standard deviation by the average, and multiplying×100.

[0013] FIGS. **4**A-C are charts showing stimulation of endothelial cell proliferation and VEGF secretion by ASC (A-B), and IL-10 secretion by monocytes coincubated with ASC (C) for 3 representative batches of placental ASC expanded as described for FIG. **3**. For A and C, the vertical axis is percentage activity of the reference batch; while for B, the vertical axis shows picograms per milliliter (pg/ml) of VEGF.

[0014] FIGS. **5**A-C are charts showing percent viability (A), percent recovery (B) and percent of cell adhesion (C) of the 3 representative batches examined in the previous figure.

[0015] FIG. **6** contains charts depicting the mean (A) and adjusted mean (B) log MWD change of subjects in the FAS2Rx receiving placebo (dashed line) or 2 injections of 300 million ASC from 2 different placentas (dotted line) or the same placenta (solid line). Bars depict the standard error.

[0016] FIG. **7** is a plot showing change from baseline in blood CRP (nmol/L) in subjects who received 2 doses of 300M ASC each from a different placenta (dotted line) or from the same placenta (dashed line), and the PBO-PBO group (solid line). All subjects were from the mFAS population. Vertical axis: adjusted means+/−SE of change in blood CRP (nmol/L). Horizontal axis: study week. One asterisk (*) indicates p=0.040 (ASC from 1 donor vs ASC from 2 donors), whereas two asterisks (**) indicate p=0.038 (ASC from 1 donor vs ASC from 2 donors) and p=0.0012 (PBO-PBO vs ASC from 2 donors).

DETAILED DESCRIPTION

[0017] Before explaining at least one embodiment of the invention in detail, it is to be understood that the invention is not limited in its application to the details set forth in the following description or exemplified by the Examples. The invention is capable of other embodiments or of being practiced or carried out in various ways. Also, it is to be understood that the phraseology and terminology employed herein is for the purpose of description and should not be regarded as limiting.

[0018] Aspects of the invention relate to methods and compositions that comprise placental adherent stromal cells (ASC). In certain embodiments, the cells are allogeneic. In other embodiments, the cells may be autologous. Alternatively or in addition, the cells may be fresh or, in other embodiments, frozen (for example, cryo-preserved). Allogeneic, as used herein (except where indicated otherwise), refers to a biological material (e.g. ASC) not derived from, and not syngeneic with, the subject being treated. Typically, allogeneic ASC are neither syngeneic nor haploidentical with the subject. In some embodiments, the described ASC are allogeneic human ASC.